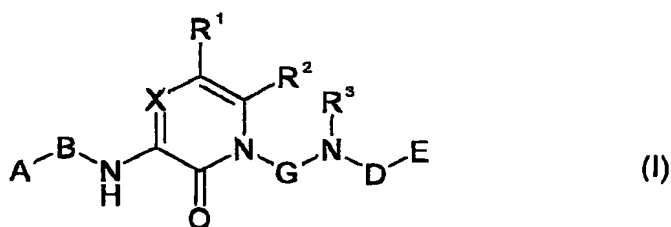


AMENDED CLAIMS

[received by the International Bureau on 16 March 2005 (16.03.05);
original claims 1-30 replaced by amended claims 1-32]

1. A compound of Formula (I)



or a pharmaceutically acceptable salt thereof, wherein:

R¹ is hydrogen;

CN;

halogen; or

C₁₋₄ alkyl, optionally substituted with one or more fluoro;

R² is hydrogen;

CN;

halogen; or

C₁₋₆ alkyl substituted with one or more fluoro;

R³ is hydrogen;

C₁₋₄ alkyl; or

C₃₋₆ cycloalkyl;

A is A¹, wherein A¹ is selected from the group consisting of:

phenyl;

naphthyl;

heterocycle containing up to 4 heteroatoms, which are the same or different and

BEST AVAILABLE COPY

selected from the group consisting of -O-, -S-, -S(O)-, -S(O₂)-, -N=, -N(O)= and -N(R⁴)-; and

heterobicycles containing up to 6 heteroatoms, which are the same or different

and selected from the group consisting of -O-, -S-, -S(O)-, -S(O₂)-, -N=, -N(O)= and -N(R⁴)-;

wherein A¹ is optionally substituted with one or independently from each other more of

A²;

A³;

halogen;

CN;

-N(R⁵R⁶);

-OH;

=O, where the ring is at least partially saturated;

C₃₋₈ cycloalkyl;

-COOR⁷; or

-CONR⁸R⁹;

-S(O)₂NR^{8a}R^{9a}

and wherein R⁴, R⁵, R⁶ are independently selected from the group consisting of R^{7a}, -C(O)-R^{7a}, -C(O)O-R^{7a}, -C(O)NR^{7a}R^{7b}, -S(O)₂NR^{7a}R^{7b}, and S(O)₂-R^{7a};

and wherein R⁷, R^{7a}, R^{7b}, R⁸, R^{8a}, R⁹, R^{9a} are independently hydrogen or C₁₋₄ alkyl, wherein each C₁₋₄ alkyl is optionally substituted with one or more substituents independently selected from the group consisting of -COOH; -OH; -NH₂; -NH-C₁₋₄ alkyl; -N(C₁₋₄ alkyl)₂; and C₃₋₈ cycloalkyl;

Optionally R⁴ is a bond to directly attach A to B;

A² is selected from the group consisting of A⁴, -O-A⁴ and -N(R¹⁰)-A⁴,

wherein A⁴ is phenyl or a heterocycle containing up to 4 heteroatoms, which are the same or different and selected from the group consisting of -O-, -S-, -S(O)-, -S(O₂)-, -N=, -N(O)= and -N(R¹¹)-; wherein A⁴ is optionally substituted with one or independently from each other more of

fluoro;

chloro;

-N(R¹²R¹³)

C₁₋₄ alkyl or -O-C₁₋₄ alkyl, both optionally substituted with one or independently from each other more of fluoro or -N(R¹⁴R¹⁵);
 and wherein R¹⁰, R¹², R¹³, R¹⁴, R¹⁵ are independently hydrogen or C₁₋₄ alkyl;
 and wherein R¹¹ is selected from the group consisting of hydrogen, C₁₋₄ alkyl
 and -C(O)-C₁₋₄ alkyl;

A³ is selected from the group consisting of C₁₋₆ alkyl, -O-C₁₋₆ alkyl and -N(R¹⁶)-C₁₋₆ alkyl, wherein the C₁₋₆ alkyl group is optionally substituted with one or independently from each other more of

fluoro;
 -N(R¹⁷R¹⁸);
 A⁵;
 and/or A³ is optionally interrupted with one or more oxygen;
 and wherein R¹⁶, R¹⁷, R¹⁸ are independently hydrogen or C₁₋₄alkyl;

A⁵ is phenyl or a heterocycle containing up to 4 heteroatoms, which are the same or different and selected from the group consisting of -O-, -S-, -S(O)-, -S(O₂)-, -N=, -N(O)= and -N(R¹⁹)-; wherein A⁵ is optionally substituted with one or independently from each other more of

fluoro;
 chloro;
 -N(R²⁰R²¹)

C₁₋₄ alkyl or -O-C₁₋₄ alkyl, both optionally substituted with one or independently from each other more of fluoro or -N(R²²R²³);
 and wherein R¹⁹ is selected from the group consisting of hydrogen, C₁₋₄ alkyl
 and -C(O)-C₁₋₄ alkyl;
 and wherein R²⁰, R²¹, R²², R²³ are independently hydrogen or C₁₋₄ alkyl;

B is selected from the group consisting of -Y-Z-; -Y-Z-C(O)-; -Y-Z-O-C(O)-; -Y-Z-S(O)₂-; and -Y-Z-NH-C(O)- wherein

Y is a bond, -O-, -S-, -N(R²⁴)-, -N(R²⁵)-C(O)-, -C(O)-N(R²⁶)-, or -C(O)-;

Z is C₁₋₆ alkyl,

optionally interrupted with oxygen, sulfur or -N(R²⁷)-
 and/or optionally substituted with one or independently from each other more of
 halogen;

CN;

C₃₋₆ cycloalkyl;

-COOR²⁸;

-CON(R²⁹R³⁰)

and/or optionally one chain carbon forms part of a C₃₋₆ cycloalkyl;
and wherein R²⁴, R²⁵, R²⁶, R²⁷, R²⁸, R²⁹, R³⁰ are independently
hydrogen; or

C₁₋₄ alkyl, optionally substituted with -COOR³¹ or -CON(R³²R³³)

wherein R³¹, R³², R³³ are independently hydrogen, or
C₁₋₄ alkyl;

X is =C(R³⁴)- or =N-, wherein R³⁴ is
hydrogen;

C₁₋₆ alkyl, optionally substituted with one or more fluoro; or

-S(O)₂R³⁵, wherein R³⁵ is selected from the group consisting of X¹, C₁₋₅ alkyl,
and -C₁₋₆ alkyl-X¹; wherein R³⁵ is optionally substituted with one or
independently from each other more of

fluoro;

chloro;

C₁₋₄ alkyl; or

-O-C₁₋₄ alkyl;

X¹ is phenyl or heterocycle containing up to 4 heteroatoms, which are the same or different
and selected from the group consisting of -O-, -S-, -S(O)-, -S(O)₂-, -N=, -N(O)= and -N(R³⁶)-;
and wherein R³⁶ is selected from the group consisting of hydrogen,
C₁₋₄ alkyl and -C(O)-C₁₋₄ alkyl;

G is -CH(R³⁷)-C(R³⁸R³⁹)-;

-CH(R³⁷)-C(R³⁸R³⁹)-C(R⁴⁰R⁴¹)-;

wherein R³⁷, R³⁸, R³⁹, R⁴⁰, R⁴¹ are independently
hydrogen;

C₁₋₄ alkyl, optionally substituted with one or more fluoro;

C₃₋₆ cycloalkyl, optionally substituted with one or more fluoro;

or R³⁸ and R³⁹ or R⁴⁰ and R⁴¹ form together C₃₋₆ cycloalkyl, optionally
substituted with one or more fluoro, -OH, C₁₋₄ alkyl;

or R³⁷ and R³⁸ or R³⁸ and R⁴⁰ form together C₃₋₆ cycloalkyl, optionally substituted with one or more fluoro, -OH, C₁₋₄ alkyl;

D is C₁₋₆ alkyl,
optionally interrupted with oxygen, sulfur or -N(R⁴²)-
and/or optionally substituted with halogen, CN, C₃₋₆ cycloalkyl;
and/or optionally one chain carbon or two vicinal carbons form part of a C₃₋₆ cycloalkyl, wherein R⁴² is selected from the group consisting of hydrogen, C₁₋₄ alkyl, C₃₋₆ cycloalkyl and -C(O)-C₁₋₄ alkyl;

E is E¹, wherein E¹ is selected from the group consisting of
phenyl;
naphthyl;
heterocycle containing up to 4 heteroatoms, which are the same or different and
selected from the group consisting of -O-, -S-, -S(O)-, -S(O₂)-, -N=,
-N(O)= and -N(R⁴³)-; and
heterobicycle containing up to 6 heteroatoms, which are the same or different
and selected from the group consisting of -O-, -S-, -S(O)-, -S(O₂)-, -N=,
-N(O)= and -N(R⁴⁴)-;
wherein E¹ is optionally substituted with one or independently from each other more
of

E²;

E³;

halogen;

CN;

-N(R⁴⁵R⁴⁶);

-OH;

=O, where the ring is at least partially saturated;

C₃₋₆ cycloalkyl;

-COOR⁴⁷; or

-CONR⁴⁸R⁴⁹;

-S(O)₂NR^{48a}R^{48b};

and wherein R⁴³, R⁴⁴, R⁴⁵, R⁴⁶ are independently selected from the group consisting of
hydrogen;

C₁₋₄ alkyl optionally substituted with -OH;

and -C(O)-C₁₋₄ alkyl optionally substituted with -OH;
 and wherein R⁴⁷, R⁴⁸, R^{48a}, R⁴⁹, R^{49a} are independently hydrogen or C₁₋₄ alkyl, optionally substituted with -OH;

E² is selected from the group consisting of E⁴, -C(O)-E⁴, -O-E⁴ and -N(R⁵⁰)-E⁴,

wherein E⁴ is phenyl or heterocycle containing up to 4 heteroatoms, which are the same or different and selected from the group consisting of -O-, -S-, -S(O)-, -S(O₂)-, -N=, -N(O)= and -N(R⁵¹)-; wherein E⁴ is optionally substituted with one or independently from each other more of

fluoro;
 chloro;
 cyano;
 =O, where the ring is at least partially saturated;
 -N(R⁵²R⁵³);
 C₁₋₄ alkyl; or
 -O-C₁₋₄ alkyl;

and wherein R⁵⁰, R⁵², R⁵³ are independently hydrogen or C₁₋₄ alkyl, optionally substituted with -OH;

and wherein R⁵¹ is selected from the group consisting of

hydrogen;
 C₁₋₄ alkyl, optionally substituted with -OH; and
 -C(O)-C₁₋₄ alkyl, optionally substituted with -OH;

E³ is selected from the group consisting of C₁₋₆ alkyl, -O-C₁₋₆ alkyl; -N(R⁵⁴)-C₁₋₆ alkyl, wherein E³ is optionally substituted with one or independently from each other more of

fluoro;
 -N(R⁵⁵R⁵⁶);
 E⁵;

and/or E³ is optionally interrupted with one or more oxygen;
 and wherein R⁵⁴, R⁵⁵, R⁵⁶ are independently hydrogen or C₁₋₄alkyl, optionally substituted with -OH;

E^5 is phenyl or heterocycle containing up to 4 heteroatoms, which are the same or different and selected from the group consisting of -O-, -S-, -S(O)-, -S(O)₂-, -N=, -N(O)= and -N(R⁵⁷)-; wherein E^5 is optionally substituted with one or independently from each other more of

fluoro;

chloro;

cyano;

=O, where the ring is at least partially saturated;

-N(R⁵⁸R⁵⁹);

C₁₋₄ alkyl or

-O-C₁₋₄ alkyl;

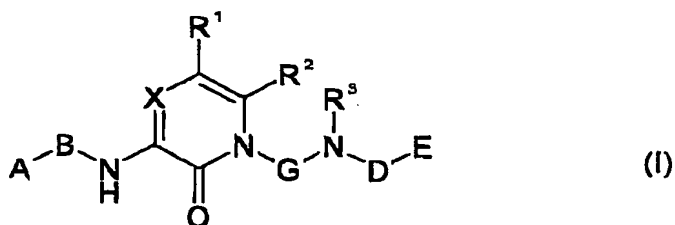
and wherein R⁵⁷ is independently selected from the group consisting of hydrogen;

C₁₋₄ alkyl, optionally substituted with -OH; and

-C(O)-C₁₋₄ alkyl, optionally substituted with -OH;

and wherein R⁵⁸, R⁵⁹ are independently hydrogen or C₁₋₄ alkyl, optionally substituted with -OH.

2. A compound of Formula (I)



or a pharmaceutically acceptable salt thereof, wherein:

R¹ is hydrogen;

CN;

halogen; or

C₁₋₄ alkyl, optionally substituted with one or more fluoro;

R² is hydrogen;

halogen;

CN;

C₁₋₆ alkyl, optionally substituted with one or more fluoro;

C₃₋₆ cycloalkyl; or
O-C₁₋₄ alkyl;

R³ is hydrogen;
C₁₋₄ alkyl; or
C₃₋₆ cycloalkyl;

A is A¹, wherein A¹ is selected from the group consisting of:
phenyl;
naphthyl;
heterocycle containing up to 4 heteroatoms, which are the same or different and
selected from the group consisting of -O-, -S-, -S(O)-, -S(O₂)-, -N=, -N(O)= and -N(R⁴)-; and
heterobicycles containing up to 6 heteroatoms, which are the same or different
and selected from the group consisting of -O-, -S-, -S(O)-, -S(O₂)-, -N=, -N(O)= and -N(R⁴)-;
wherein A¹ is optionally substituted with one or independently from each other more of
A²;
A³;
halogen;
CN;
-N(R⁵R⁶);
-OH;
=O, where the ring is at least partially saturated;
C₃₋₆ cycloalkyl;
-COOR⁷; or
-CONR⁸R⁹;
-S(O)₂NR^{8a}R^{9a};
and wherein R⁴, R⁵, R⁶ are independently selected from the group consisting of R^{7a}, -C(O)-R^{7a}, -C(O)O-R^{7a}, -C(O)NR^{7a}R^{7b}, -S(O)₂NR^{7a}R^{7b}, and S(O)₂-R^{7a};
and wherein R⁷, R^{7a}, R^{7b}, R⁸, R^{8a}, R⁹, R^{9a} are independently hydrogen or C₁₋₄ alkyl,
wherein each C₁₋₄ alkyl is optionally substituted with one or more substituents
independently selected from the group consisting of -COOH; -OH; -NH₂;
-NH-C₁₋₄ alkyl; -N(C₁₋₄ alkyl)₂; and C₃₋₆ cycloalkyl;

Optionally R^4 is a bond to directly attach A to B;

A^2 is selected from the group consisting of A^4 , $-O-A^4$ and $-N(R^{10})-A^4$,

wherein A^4 is phenyl or a heterocycle containing up to 4 heteroatoms, which are the same or different and selected from the group consisting of $-O-$, $-S-$, $-S(O)-$, $-S(O_2)-$, $-N=$, $-N(O)=$ and $-N(R^{11})-$; wherein A^4 is optionally substituted with one or independently from each other more of

fluoro;

chloro;

$-N(R^{12}R^{13})$

C_{1-4} alkyl or $-O-C_{1-4}$ alkyl, both optionally substituted with one or independently from each other more of fluoro or $-N(R^{14}R^{15})$;

and wherein R^{10} , R^{12} , R^{13} , R^{14} , R^{15} are independently hydrogen or C_{1-4} alkyl;

and wherein R^{11} is selected from the group consisting of hydrogen, C_{1-4} alkyl and $-C(O)-C_{1-4}$ alkyl;

A^3 is selected from the group consisting of C_{1-6} alkyl, $-O-C_{1-6}$ alkyl and $-N(R^{16})-C_{1-6}$ alkyl, wherein the C_{1-6} alkyl group is optionally substituted with one or independently from each other more of

fluoro;

$-N(R^{17}R^{18})$;

A^5 ;

and/or A^3 is optionally interrupted with one or more oxygen;

and wherein R^{16} , R^{17} , R^{18} are independently hydrogen or C_{1-4} alkyl;

A^5 is phenyl or a heterocycle containing up to 4 heteroatoms, which are the same or different and selected from the group consisting of $-O-$, $-S-$, $-S(O)-$, $-S(O_2)-$, $-N=$, $-N(O)=$ and $-N(R^{19})-$; wherein A^5 is optionally substituted with one or independently from each other more of

fluoro;

chloro;

$-N(R^{20}R^{21})$

C_{1-4} alkyl or $-O-C_{1-4}$ alkyl, both optionally substituted with one or independently from each other more of fluoro or $-N(R^{22}R^{23})$;

and wherein R^{19} is selected from the group consisting of hydrogen, C_{1-4} alkyl

and $-C(O)-C_{1-4}$ alkyl;

and wherein R^{20} , R^{21} , R^{22} , R^{23} are independently hydrogen or C_{1-4} alkyl;

B is selected from the group consisting of $-Y-Z$; $-Y-Z-C(O)-$; $-Y-Z-O-C(O)-$; $-Y-Z-S(O)_2-$; and $-Y-Z-NH-C(O)-$ wherein

Y is a bond, $-O-$, $-S-$, $-N(R^{24})-$, $-N(R^{25})-C(O)-$, $-C(O)-N(R^{26})-$, or $-C(O)-$;

Z is C_{1-6} alkyl,

optionally interrupted with oxygen, sulfur or $-N(R^{27})-$

and/or optionally substituted with one or independently from each other more of

halogen;

CN;

C_{3-6} cycloalkyl;

$-COOR^{28}$;

$-CON(R^{29}R^{30})$

and/or optionally one chain carbon forms part of a C_{3-6} cycloalkyl;

and wherein R^{24} , R^{25} , R^{26} , R^{27} , R^{28} , R^{29} , R^{30} are independently

hydrogen; or

C_{1-4} alkyl, optionally substituted with $-COOR^{31}$ or $-CON(R^{32}R^{33})$

wherein R^{31} , R^{32} , R^{33} are independently hydrogen or C_{1-4} alkyl;

X is $=C(R^{34})-$ or $=N-$, wherein R^{34} is

hydrogen;

C_{1-6} alkyl, optionally substituted with one or more fluoro; or

$-S(O)_2R^{35}$, wherein R^{35} is selected from the group consisting of X^1 , C_{1-6} alkyl,

and $-C_{1-6}$ alkyl- X^1 ; wherein R^{35} is optionally substituted with one or

independently from each other more of

fluoro;

chloro;

C_{1-4} alkyl; or

$-O-C_{1-4}$ alkyl;

X^1 is phenyl or heterocycle containing up to 4 heteroatoms, which are the same or different and selected from the group consisting of $-O-$, $-S-$, $-S(O)-$, $-S(O)_2-$, $-N=$, $-N(O)=$ and $-N(R^{36})-$;

and wherein R^{36} is selected from the group consisting of hydrogen, C_{1-4} alkyl and $-C(O)-C_{1-4}$ alkyl;

G is $-CH(R^{37})-C(R^{38}R^{39})-$;

$-CH(R^{37})-C(R^{38}R^{39})-C(R^{40}R^{41})-$;

wherein R^{37} , R^{38} , R^{39} , R^{40} , R^{41} are independently

hydrogen;

C_{1-4} alkyl, optionally substituted with one or more fluoro;

C_{3-6} cycloalkyl, optionally substituted with one or more fluoro;

or R^{38} and R^{39} or R^{40} and R^{41} form together C_{3-6} cycloalkyl, optionally substituted with one or more fluoro, $-OH$, C_{1-4} alkyl;

or R^{37} and R^{38} or R^{38} and R^{40} form together C_{3-6} cycloalkyl, optionally substituted with one or more fluoro, $-OH$, C_{1-4} alkyl;

D is C_{1-6} alkyl,

optionally interrupted with oxygen, sulfur or $-N(R^{42})-$

and/or optionally substituted with halogen, CN, C_{3-6} cycloalkyl;

and/or optionally one chain carbon or two vicinal carbons form part of a C_{3-6} cycloalkyl, wherein R^{42} is selected from the group consisting of hydrogen, C_{1-4} alkyl, C_{3-6} cycloalkyl and $-C(O)-C_{1-4}$ alkyl;

E is E^1 , wherein E^1 is selected from the group consisting of

naphthyl;

non-aromatic heterocycle containing up to 4 heteroatoms, which are the same or different and

selected from the group consisting of $-O-$, $-S-$, $-S(O)-$, $-S(O_2)-$, $-N=$, $-N(O)=$ and $-N(R^{43})-$; and

heterobicyclic containing up to 6 heteroatoms, which are the same or different

and selected from the group consisting of $-O-$, $-S-$, $-S(O)-$, $-S(O_2)-$, $-N=$, $-N(O)=$ and $-N(R^{44})-$;

wherein E^1 is optionally substituted with one or independently from each other more of

E^2 ;

E^3 ;

halogen;

CN;
 -N(R⁴⁵R⁴⁶);
 -OH;
 =O, where the ring is at least partially saturated;
 C₃₋₆ cycloalkyl;
 -COOR⁴⁷; or
 -CONR⁴⁸R⁴⁹;
 -S(O)₂NR^{48a}R^{49a};

and wherein R⁴³, R⁴⁴, R⁴⁵, R⁴⁶ are independently selected from the group consisting of hydrogen;

C₁₋₄ alkyl optionally substituted with -OH;

and -C(O)-C₁₋₄ alkyl optionally substituted with -OH;

and wherein R⁴⁷, R⁴⁸, R^{48a}, R⁴⁹, R^{49a} are independently hydrogen or C₁₋₄ alkyl, optionally substituted with -OH;

E² is selected from the group consisting of E⁴, -C(O)-E⁴, -O-E⁴ and -N(R⁵⁰)-E⁴,

wherein E⁴ is phenyl or heterocycle containing up to 4 heteroatoms, which are the same or different and selected from the group consisting of -O-, -S-, -S(O)-, -S(O₂)-, -N=, -N(O)=, and -N(R⁵¹)-; wherein E⁴ is optionally substituted with one or independently from each other more of

fluoro;

chloro;

cyano;

=O, where the ring is at least partially saturated;

-N(R⁵²R⁵³);

C₁₋₄ alkyl; or

-O-C₁₋₄ alkyl;

and wherein R⁵⁰, R⁵², R⁵³ are independently hydrogen or C₁₋₄ alkyl, optionally substituted with -OH;

and wherein R⁵¹ is selected from the group consisting of hydrogen;

C₁₋₄ alkyl, optionally substituted with -OH; and

-C(O)-C₁₋₄ alkyl, optionally substituted with -OH;

E^3 is selected from the group consisting of C_{1-6} alkyl, $-O-C_{1-6}$ alkyl, $-N(R^{54})-C_{1-6}$ alkyl, wherein E^3 is optionally substituted with one or independently from each other more of

fluoro;

$-N(R^{55}R^{56})$;

E^5 ;

and/or E^3 is optionally interrupted with one or more oxygen;

and wherein R^{54} , R^{55} , R^{56} are independently hydrogen or C_{1-4} alkyl, optionally substituted with $-OH$;

E^5 is phenyl or heterocycle containing up to 4 heteroatoms, which are the same or different and selected from the group consisting of $-O-$, $-S-$, $-S(O)-$, $-S(O)_2-$, $-N=$, $-N(O)=$ and $-N(R^{57})-$; wherein E^5 is optionally substituted with one or independently from each other more of

fluoro;

chloro;

cyano;

$=O$, where the ring is at least partially saturated;

$-N(R^{58}R^{59})$;

C_{1-4} alkyl or

$-O-C_{1-4}$ alkyl;

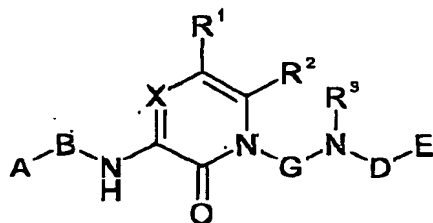
and wherein R^{57} is independently selected from the group consisting of hydrogen;

C_{1-4} alkyl, optionally substituted with $-OH$; and

$-C(O)-C_{1-4}$ alkyl, optionally substituted with $-OH$;

and wherein R^{58} , R^{59} are independently hydrogen or C_{1-4} alkyl, optionally substituted with $-OH$.

3. A compound of Formula (I)



(I)

or a pharmaceutically acceptable salt thereof, wherein:

R¹ is hydrogen;
 CN;
 halogen; or
 C₁₋₄ alkyl, optionally substituted with one or more fluoro;

R² is hydrogen;
 CN;
 halogen;
 C₁₋₈ alkyl, optionally substituted with one or more fluoro;
 C₃₋₆ cycloalkyl; or
 O-C₁₋₄ alkyl;

R³ is hydrogen;
 C₁₋₄ alkyl; or
 C₃₋₆ cycloalkyl;

A is A¹, wherein A¹ is selected from the group consisting of:
 naphthyl;
 heterocycle containing up to 4 heteroatoms, which are the same or different and
 selected from the group consisting of -S(O)-, -S(O₂)- and -N(O)=; and
 heterobicycles containing up to 6 heteroatoms, which are the same or different
 and selected from the group consisting of -O-, -S-, -S(O)-, -S(O₂)-, -N=,
 -N(O)= and -N(R⁴)-;
 wherein A¹ is optionally substituted with one or independently from each other
 more of
 A²;
 A³;
 halogen;
 CN;
 -N(R⁵R⁶);
 -OH;
 =O, where the ring is at least partially saturated;
 C₃₋₆ cycloalkyl;
 -COOR⁷; or

-CONR⁸R⁹;

-S(O)₂NR^{8a}R^{8a}

and wherein R⁴, R⁵, R⁶ are independently selected from the group consisting of: R^{7a}, -C(O)-R^{7a}, -C(O)O-R^{7a}, -C(O)NR^{7a}R^{7b}, -S(O)₂NR^{7a}R^{7b}, and S(O)₂-R^{7a};

and wherein R⁷, R^{7a}, R^{7b}, R⁸, R^{8a}, R⁹, R^{9a} are independently hydrogen or C₁₋₄ alkyl, wherein each C₁₋₄ alkyl is optionally substituted with one or more substituents independently selected from the group consisting of -COOH; -OH; -NH₂; -NH-C₁₋₄ alkyl; -N(C₁₋₄ alkyl)₂; and C₃₋₆ cycloalkyl;

Optionally R⁴ is a bond to directly attach A to B;

A² is selected from the group consisting of A⁴, -O-A⁴ and -N(R¹⁰)-A⁴,

wherein A⁴ is phenyl or a heterocycle containing up to 4 heteroatoms, which are the same or different and selected from the group consisting of -O-, -S-, -S(O)-, -S(O)₂-, -N=, -N(O)= and -N(R¹¹)-; wherein A⁴ is optionally substituted with one or independently from each other more of

fluoro;

chloro;

-N(R¹²R¹³)

C₁₋₄ alkyl or -O-C₁₋₄ alkyl, both optionally substituted with one or independently from each other more of fluoro or -N(R¹⁴R¹⁵);

and wherein R¹⁰, R¹², R¹³, R¹⁴, R¹⁵ are independently hydrogen or C₁₋₄ alkyl;

and wherein R¹¹ is selected from the group consisting of hydrogen, C₁₋₄ alkyl and -C(O)-C₁₋₄ alkyl;

A³ is selected from the group consisting of C₁₋₆ alkyl, -O-C₁₋₆ alkyl and -N(R¹⁶)-C₁₋₆ alkyl; wherein the C₁₋₆ alkyl group is optionally substituted with one or independently from each other more of

fluoro;

-N(R¹⁷R¹⁸);

A⁵;

and/or A³ is optionally interrupted with one or more oxygen;

and wherein R¹⁶, R¹⁷, R¹⁸ are independently hydrogen or C₁₋₄alkyl;

A⁵ is phenyl or a heterocycle containing up to 4 heteroatoms, which are the same or different and selected from the group consisting of -O-, -S-, -S(O)-, -S(O)₂-, -N=, -N(O)= and -N(R¹⁹)-; wherein A⁵ is optionally substituted with one or independently from each other more of

fluoro;

chloro;

-N(R²⁰R²¹);

C₁₋₄ alkyl or -O-C₁₋₄ alkyl, both optionally substituted with one or independently from each other more of fluoro or -N(R²²R²³);

and wherein R¹⁹ is selected from the group consisting of hydrogen, C₁₋₄ alkyl

and -C(O)-C₁₋₄ alkyl;

and wherein R²⁰, R²¹, R²², R²³ are independently hydrogen or C₁₋₄ alkyl;

B is selected from the group consisting of -Y-Z-, -Y-Z-C(O)-, -Y-Z-O-C(O)-, -Y-Z-S(O)₂-, and -Y-Z-NH-C(O)- wherein

Y is a bond, -O-, -S-, -N(R²⁴)-, -N(R²⁵)-C(O)-, -C(O)-N(R²⁶)-, or -C(O)-;

Z is C₁₋₆ alkyl,

optionally interrupted with oxygen, sulfur or -N(R²⁷)-

and/or optionally substituted with one or independently from each other more of

halogen;

CN;

C₃₋₆ cycloalkyl;

-COOR²⁸;

-CON(R²⁹R³⁰);

and/or optionally one chain carbon forms part of a C₃₋₆ cycloalkyl;

and wherein R²⁴, R²⁵, R²⁶, R²⁷, R²⁸, R²⁹, R³⁰ are independently

hydrogen; or

C₁₋₄ alkyl, optionally substituted with -COOR³¹ or -CON(R³²R³³)

wherein R³¹, R³², R³³ are independently hydrogen; or

C₁₋₄ alkyl;

X is =C(R³⁴)- or =N-, wherein R³⁴ is

hydrogen;

C₁₋₆ alkyl, optionally substituted with one or more fluoro; or

-S(O)₂R³⁵, wherein R³⁵ is selected from the group consisting of X¹, C₁₋₆ alkyl,

and $-C_{1-6}$ alkyl- X^1 ; wherein R^{35} is optionally substituted with one or independently from each other more of

- fluoro;
- chloro;
- C_{1-4} alkyl; or
- $-O-C_{1-4}$ alkyl;

X^1 is phenyl or heterocycle containing up to 4 heteroatoms, which are the same or different and selected from the group consisting of $-O-$, $-S-$, $-S(O)-$, $-S(O)_2-$, $-N=$, $-N(O)=$ and $-N(R^{36})-$; and wherein R^{36} is selected from the group consisting of hydrogen, C_{1-4} alkyl and $-C(O)-C_{1-4}$ alkyl;

G is $-CH(R^{37})-C(R^{38}R^{39})-$;
 $-CH(R^{37})-C(R^{38}R^{39})-C(R^{40}R^{41})-$;
 wherein R^{37} , R^{38} , R^{39} , R^{40} , R^{41} are independently

- hydrogen;
- C_{1-4} alkyl, optionally substituted with one or more fluoro;
- C_{3-6} cycloalkyl, optionally substituted with one or more fluoro;
- or R^{38} and R^{39} or R^{40} and R^{41} form together C_{3-6} cycloalkyl, optionally substituted with one or more fluoro, $-OH$, C_{1-4} alkyl;
- or R^{37} and R^{38} or R^{38} and R^{40} form together C_{3-6} cycloalkyl, optionally substituted with one or more fluoro, $-OH$, C_{1-4} alkyl;

D is C_{1-8} alkyl,
 optionally interrupted with oxygen, sulfur or $-N(R^{42})-$
 and/or optionally substituted with halogen, CN, C_{3-6} cycloalkyl;
 and/or optionally one chain carbon or two vicinal carbons form part of a C_{3-6} cycloalkyl, wherein R^{42} is selected from the group consisting of hydrogen, C_{1-4} alkyl, C_{3-6} cycloalkyl and $-C(O)-C_{1-4}$ alkyl;

E is E^1 , wherein E^1 is selected from the group consisting of

- phenyl;
- naphthyl;
- heterocycle containing up to 4 heteroatoms, which are the same or different and

selected from the group consisting of -O-, -S-, -S(O)-, -S(O₂)-, -N=, -N(O)= and -N(R⁴³)-; and
 heterobicycle containing up to 6 heteroatoms, which are the same or different and selected from the group consisting of -O-, -S-, -S(O)-, -S(O₂)-, -N=, -N(O)= and -N(R⁴⁴)-;
 wherein E¹ is optionally substituted with one or independently from each other more of

E²;

E³;

halogen;

CN;

-N(R⁴⁵R⁴⁶);

-OH;

=O, where the ring is at least partially saturated;

C₃₋₆ cycloalkyl;

-COOR⁴⁷; or

-CONR⁴⁸R⁴⁹;

-S(O)₂NR^{48a}R^{49a};

and wherein R⁴³, R⁴⁴, R⁴⁵, R⁴⁶ are independently selected from the group consisting of hydrogen;

C₁₋₄ alkyl optionally substituted with -OH;

and -C(O)-C₁₋₄ alkyl optionally substituted with -OH;

and wherein R⁴⁷, R⁴⁸, R^{48a}, R⁴⁹, R^{49a} are independently hydrogen or C₁₋₄ alkyl, optionally substituted with -OH;

E² is selected from the group consisting of E⁴, -C(O)-E⁴, -O-E⁴ and -N(R⁵⁰)-E⁴,

wherein E⁴ is phenyl or heterocycle containing up to 4 heteroatoms, which are the same or different and selected from the group consisting of -O-, -S-, -S(O)-, -S(O₂)-, -N=, -N(O)= and -N(R⁵¹)-; wherein E⁴ is optionally substituted with one or independently from each other more of

fluoro;

chloro;

ciano;

=O, where the ring is at least partially saturated;

-N(R⁵²R⁵³);

C_{1-4} alkyl; or
 $-O-C_{1-4}$ alkyl;
 and wherein R^{50} , R^{52} , R^{53} are independently hydrogen or C_{1-4} alkyl, optionally substituted with $-OH$;
 and wherein R^{51} is selected from the group consisting of
 hydrogen;
 C_{1-4} alkyl, optionally substituted with $-OH$; and
 $-C(O)-C_{1-4}$ alkyl, optionally substituted with $-OH$;

E^3 is selected from the group consisting of C_{1-6} alkyl, $-O-C_{1-6}$ alkyl, $-N(R^{54})-C_{1-6}$ alkyl, wherein E^3 is optionally substituted with one or independently from each other more of

fluoro;
 $-N(R^{55}R^{56})$;
 E^5 ;

and/or E^3 is optionally interrupted with one or more oxygen;
 and wherein R^{54} , R^{55} , R^{56} are independently hydrogen or C_{1-4} alkyl, optionally substituted with $-OH$;

E^5 is phenyl or heterocycle containing up to 4 heteroatoms, which are the same or different and selected from the group consisting of $-O-$, $-S-$, $-S(O)-$, $-S(O_2)-$, $-N=$, $-N(O)=$ and $-N(R^{57})-$; wherein E^5 is optionally substituted with one or independently from each other more of

fluoro;
 chloro;
 cyano;
 $=O$, where the ring is at least partially saturated;
 $-N(R^{58}R^{59})$;
 C_{1-4} alkyl or
 $-O-C_{1-4}$ alkyl;

and wherein R^{57} is independently selected from the group consisting of hydrogen;
 C_{1-4} alkyl, optionally substituted with $-OH$; and
 $-C(O)-C_{1-4}$ alkyl, optionally substituted with $-OH$;
 and wherein R^{58} , R^{59} are independently hydrogen or C_{1-4} alkyl, optionally substituted with $-OH$.

4. A compound according to any of the preceding claims, wherein R^1 is hydrogen.
5. A compound according to any of the preceding claims, wherein R^2 is hydrogen, chloro, $-CH_3$, $-CH_2-CH_3$, $-CH_2-CH_2-CH_3$, $-CH_2-CH_2-CH_2-CH_3$, $-CH_2F$, $-CHF_2$ or $-CN$.
6. A compound according to any one of the preceding claims, wherein R^3 is hydrogen.
7. A compound according to any one of the preceding claims, wherein A^1 is phenyl or heterocycle containing up to 4 heteroatoms, which are the same or different and selected from the group consisting of $-O-$, $-S-$, $-S(O)-$, $-S(O)_2-$, $-N=$, $-N(O)=$ and $-N(R^4)-$, wherein R^4 has the meaning as indicated in claim 1.
8. A compound according to claim 7, wherein A^1 is selected from the group consisting of phenyl, pyridine, pyridine-N oxide, piperidine, morpholine, and pyrrolidine.
9. A compound according to any of the preceding claims, wherein R^4 is a bond, $-COOC_{1-4}$ alkyl, methyl, ethyl, 2-hydroxyethyl, $-COOH$, $-CH_2-COOH$, $-CH_2-COO-C_{1-4}$ alkyl or cyclopropylmethyl and wherein A^1 is optionally substituted with up to 4 F.
10. A compound according to any one of the preceding claims, wherein B is $-Y-Z-$.
11. A compound according to any one of the preceding claims, wherein Y is a bond, $-O-$, $-NH-$, $-S(O)_2-$ or $-C(O)-$.
12. A compound according to any one of the preceding claims, wherein Z is $-C(R^{60}R^{61})-$ or $-C(R^{60}R^{61})-C(R^{62}R^{63})-$, wherein
 R^{60} , R^{61} , R^{62} , R^{63} are independently hydrogen, $-C(O)NH_2$, $-COOH$, $-CH_2-COOH$, $-CH_2-C(O)NH_2$, fluoro, methyl, cyclopropyl or
 R^{60} and R^{61} form a cyclopropyl ring or
 R^{62} and R^{63} form a cyclopropyl ring or
 R^{60} and R^{62} form a cyclopropyl or cyclobutyl ring.
13. A compound according to claim 12, wherein R^{60} , R^{61} , R^{62} , R^{63} are independently hydrogen, fluoro or $-C(O)NH_2$.

14. A compound according to any one of the preceding claims, wherein X is =N-.
15. A compound according to any of the preceding claims, wherein G is $-\text{CH}(\text{R}^{64})-\text{C}(\text{R}^{65}\text{R}^{66})-$; wherein R^{64} , R^{65} , R^{66} are independently hydrogen, F, methyl, $-\text{CH}_2\text{F}$, $-\text{CHF}_2$, CF_3 or cyclopropyl or R^{65} , R^{66} form together cyclopropyl.
16. a compound according to any one of the preceding claims, wherein G is $-\text{CH}_2-\text{CH}_2-$.
17. A compound according to any one of the preceding claims, wherein D is $-\text{CH}_2-$, $-\text{CF}_2-$, $-\text{CH}(\text{CH}_3)-$, $-\text{C}(\text{CH}_3)_2-$ or D^1-D^2 , where D^1 and D^2 are independently $-\text{CH}_2-$, $-\text{CF}_2-$, $-\text{CH}(\text{CH}_3)-$ or $-\text{C}(\text{CH}_3)_2-$ and wherein D^2 is optionally $-\text{CH}_2-\text{NH}-$.
18. A compound according to claim 17, wherein D is $-\text{CH}_2-$, $-\text{CH}(\text{CH}_3)-$, $-\text{CH}_2-\text{CH}_2-$, $-\text{CH}_2-\text{CF}_2$ or $-\text{CH}_2-\text{CH}_2-\text{NH}-$.
19. A compound according to any one of the preceding claims, wherein -E is selected from the group consisting of phenyl; heterocycle containing up to three heteroatoms, which are the same or different and selected from the group consisting of $-\text{O}-$, $-\text{N}=\text{}$, $-\text{N}(\text{O})-$ and $-\text{NH}-$; and heterobicyclic containing up to three heteroatoms, which are the same or different and selected from the group consisting of $-\text{O}-$, $-\text{N}=\text{}$, and $-\text{NH}-$; and wherein E is optionally substituted with up to two substituents which are the same or different and selected from the group consisting of CN, F, Cl, C_{1-4} alkyl, OH, $\text{O}-\text{C}_{1-4}$ alkyl, NH_2 , $\text{NH}-\text{C}_{1-4}$ alkyl, $\text{N}(\text{C}_{1-4} \text{ alkyl})_2$, $\text{C}(\text{O})\text{NH}_2$, $\text{C}(\text{O})\text{NH}-\text{C}_{1-4}$ alkyl, and $\text{C}(\text{O})\text{N}(\text{C}_{1-4} \text{ alkyl})_2$, wherein each C_{1-4} alkyl is optionally substituted with one or more substituents independently selected from OH and F.
20. A compound according to claim 19, wherein -E is phenyl, pyridine, benzimidazole, indazole, quinoline, isoquinoline, pyridine-(N)-oxide, benzothiophene, indole, azaindole, benzofuran, benzisoxazole, benzoxazole, benzothiazole.
21. A compound according to any one of the preceding claims, wherein -E is selected from the group consisting of

$-\text{COOR}^{75}$ or $-\text{C(O)NR}^{76}\text{R}^{77}$;

and wherein R^{72} , R^{73} , R^{74} , R^{75} , R^{76} , R^{77} are independently

hydrogen;

C_{1-4} alkyl; or

$-\text{C(O)-C}_{1-4}$ alkyl;

E^6 is selected from the group consisting of C_{1-6} alkyl; $-\text{O-C}_{1-6}$ alkyl; and $-\text{N(R}^{78})-\text{C}_{1-6}$ alkyl, wherein the C_{1-6} alkyl group is optionally substituted with one or more of halogen;

CN;

$-\text{N(R}^{79}\text{R}^{80})$;

phenyl, optionally substituted with chloro;

heterocycle containing up to 4 heteroatoms, which are the same or different and selected from the group consisting of $-\text{O}-$, $-\text{S}-$, $-\text{S(O)}-$, $-\text{S(O)}_2-$, $-\text{N=}$, $-\text{N(O)=}$ and $-\text{N(R}^{81})-$, optionally substituted with chloro;

and/or E^6 is optionally interrupted by one or more of oxygen;

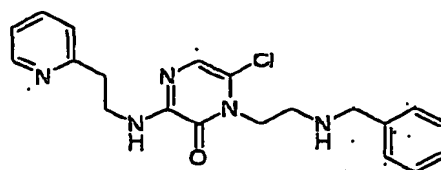
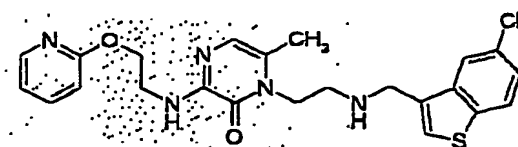
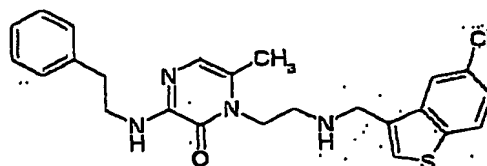
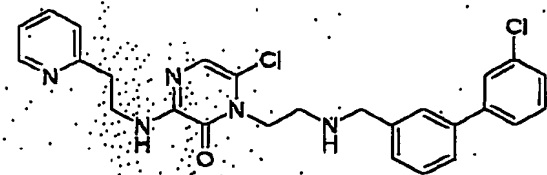
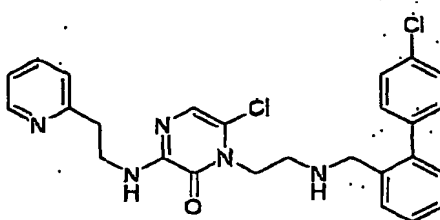
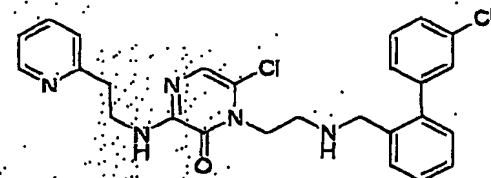
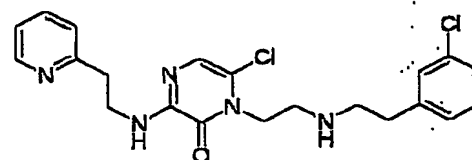
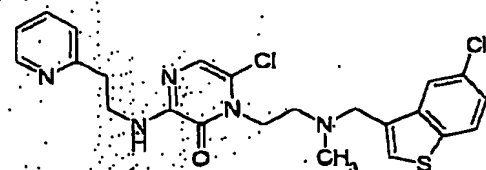
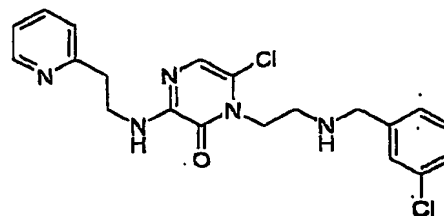
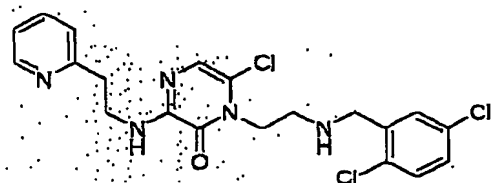
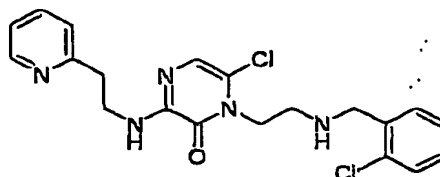
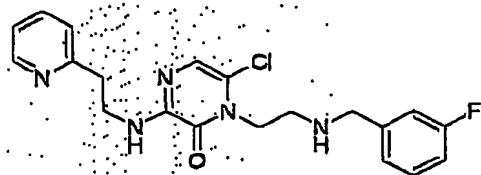
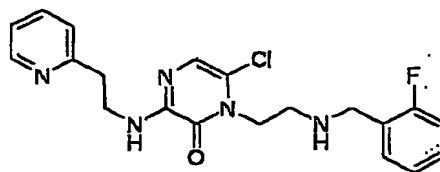
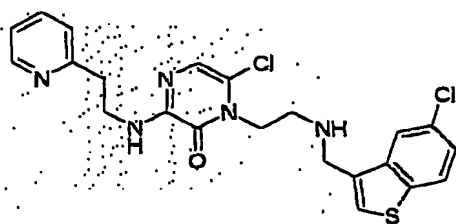
and wherein R^{78} , R^{79} , R^{80} , R^{81} are independently hydrogen, C_{1-4} alkyl;

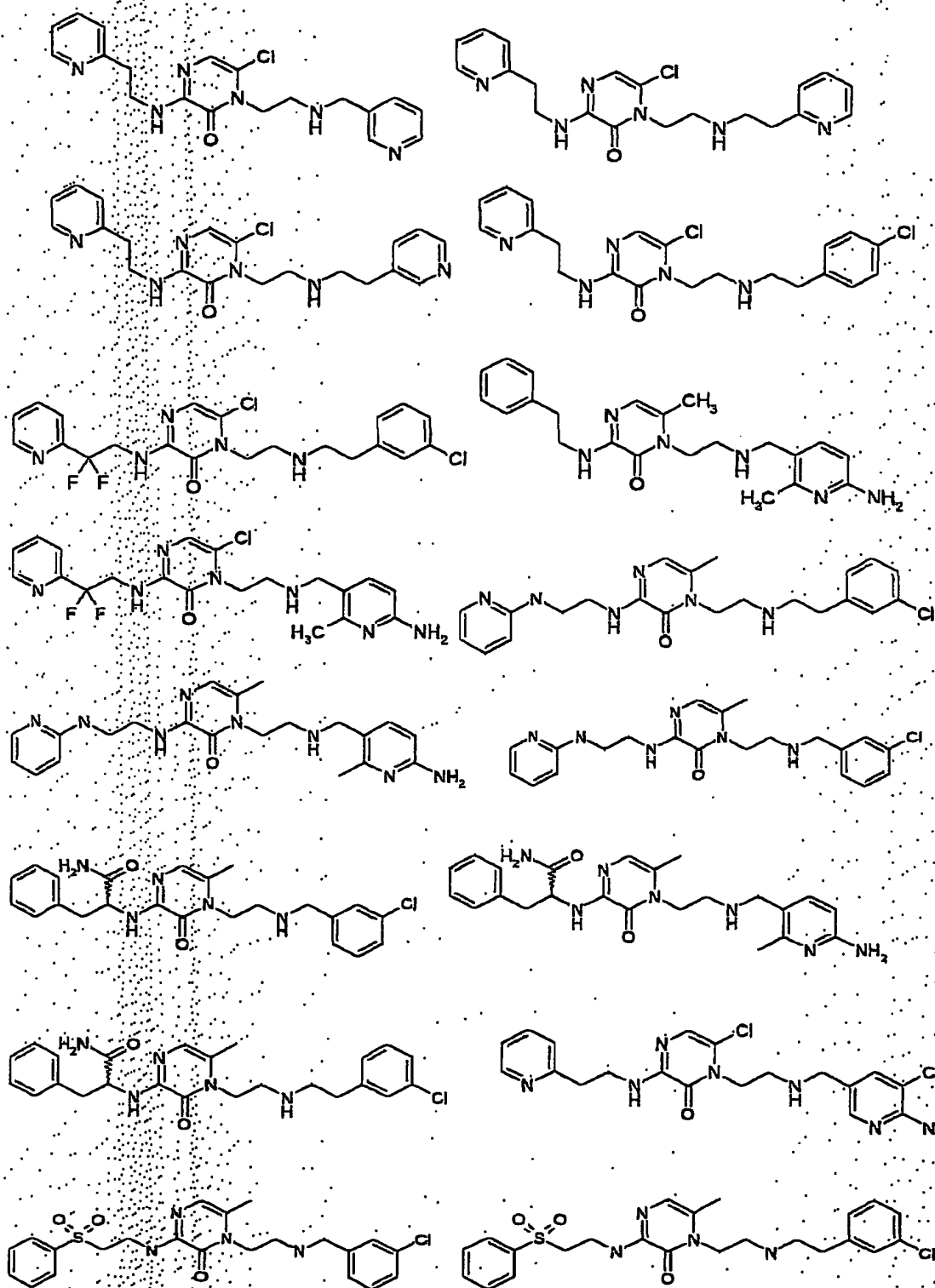
E^7 is selected from the group consisting of E^8 , $-\text{O-E}^8$, $-\text{N(R}^{82})-\text{E}^8$, and $-\text{C(O)-E}^8$, wherein E^8 is phenyl or heterocycle containing up to 4 heteroatoms, which are the same or different and selected from the group consisting of $-\text{O}-$, $-\text{S}-$, $-\text{S(O)}-$, $-\text{S(O)}_2-$, $-\text{N=}$, $-\text{N(O)=}$ and $-\text{N(R}^{83})-$, and wherein E^8 is optionally substituted with chloro or $-\text{N(R}^{84}\text{R}^{85})$;

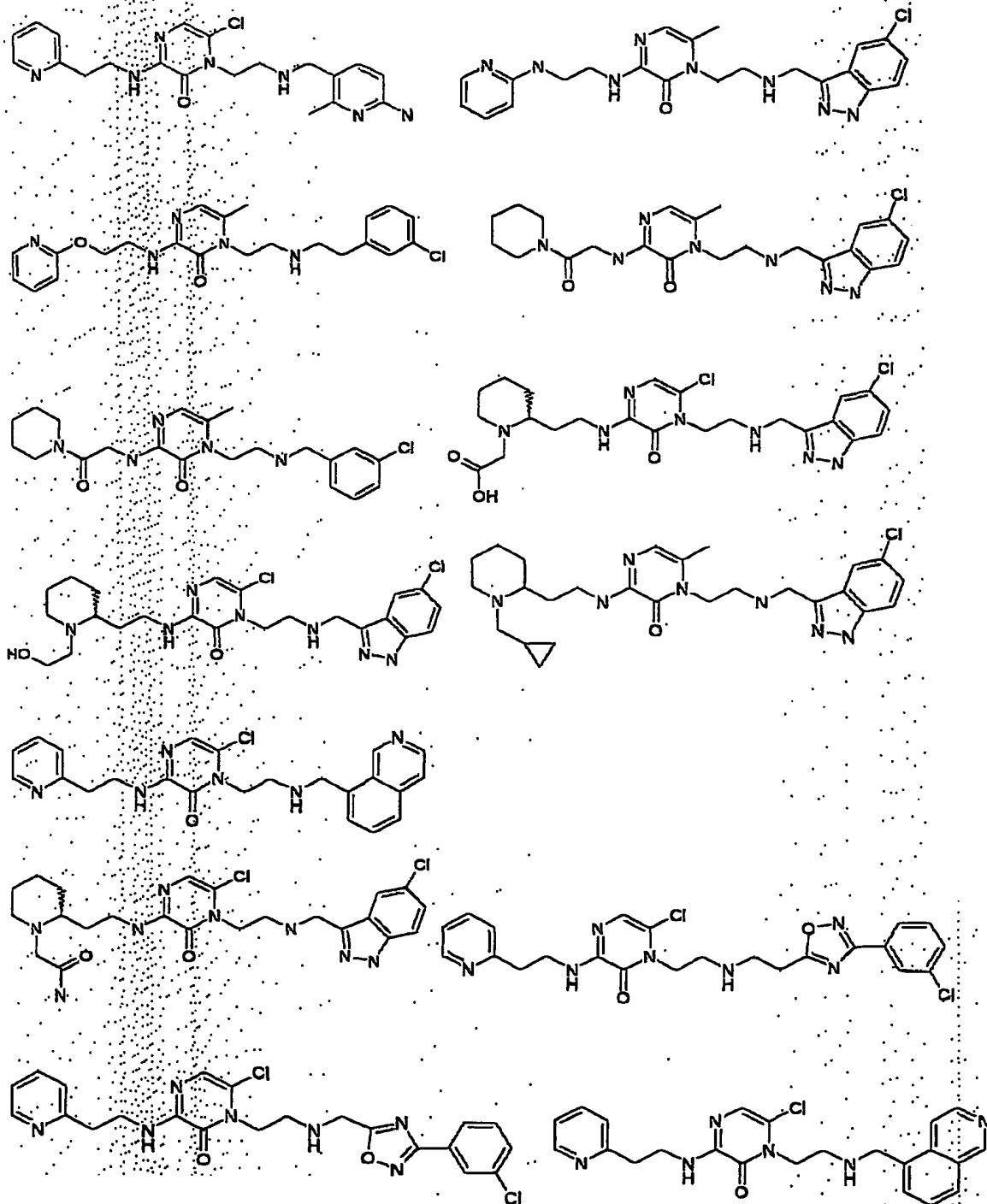
and wherein R^{82} , R^{83} , R^{84} , R^{85} are independently hydrogen or C_{1-4} alkyl.

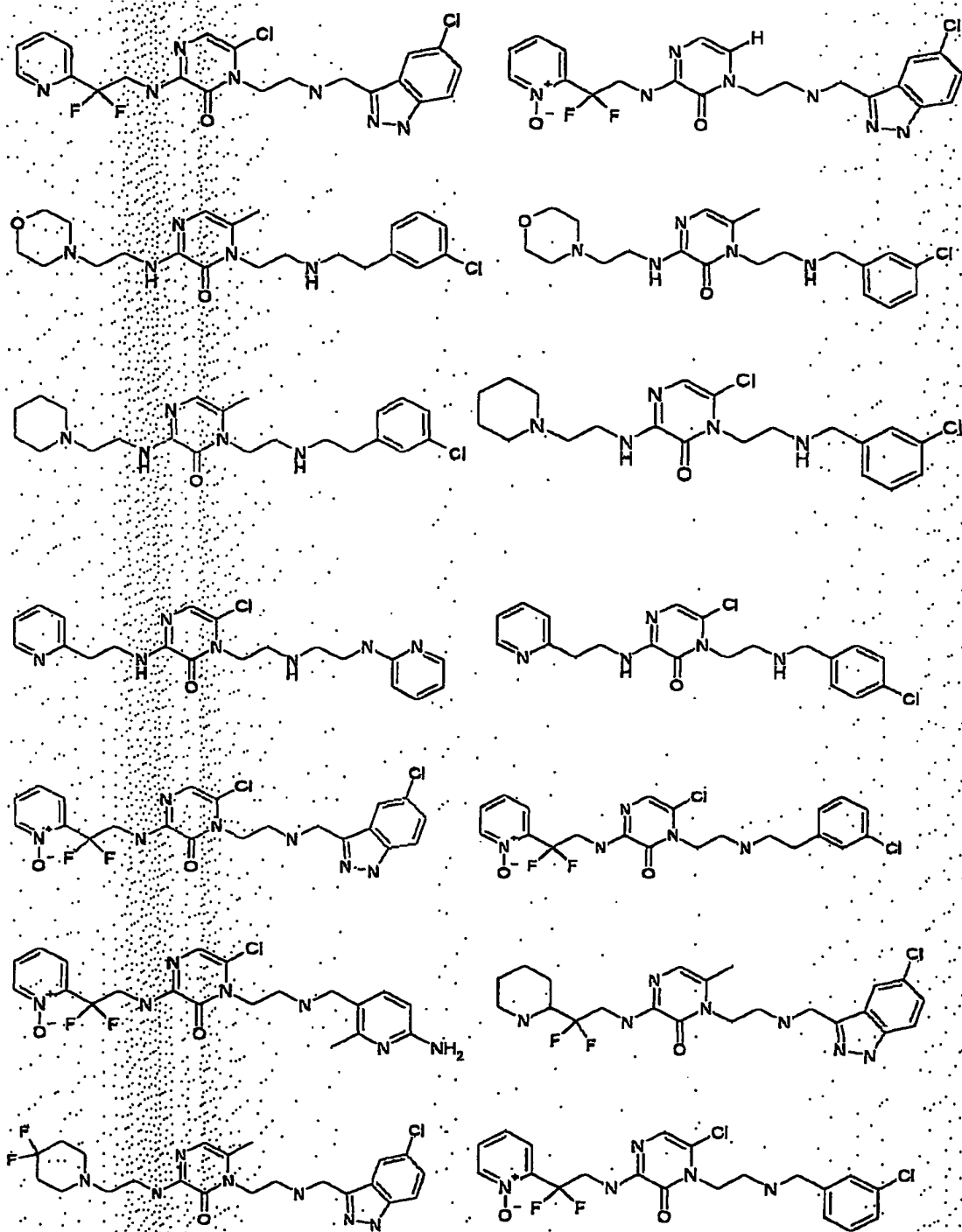
22. A compound according to claim 21, wherein R^{67} , R^{68} , R^{69} , R^{70} , R^{71} are independently selected from the group consisting of hydrogen, fluoro, chloro, cyano, phenyl, chlorophenyl, methyl, methoxy, amino, monomethyl amino, dimethyl amino, pyrrolyl, diazoly, triazolyl, and tetrazolyl.

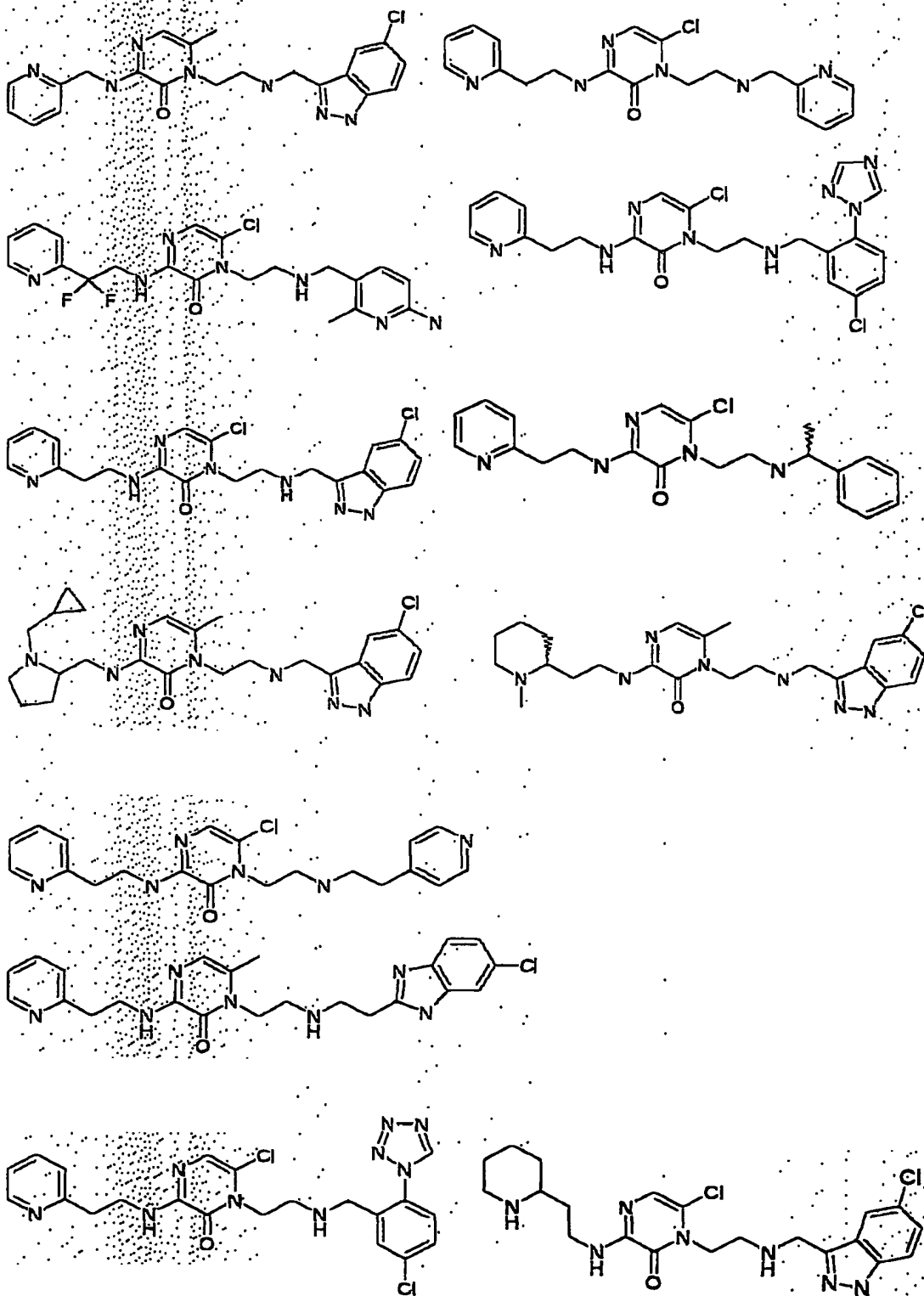
23. A compound selected from the group consisting of.

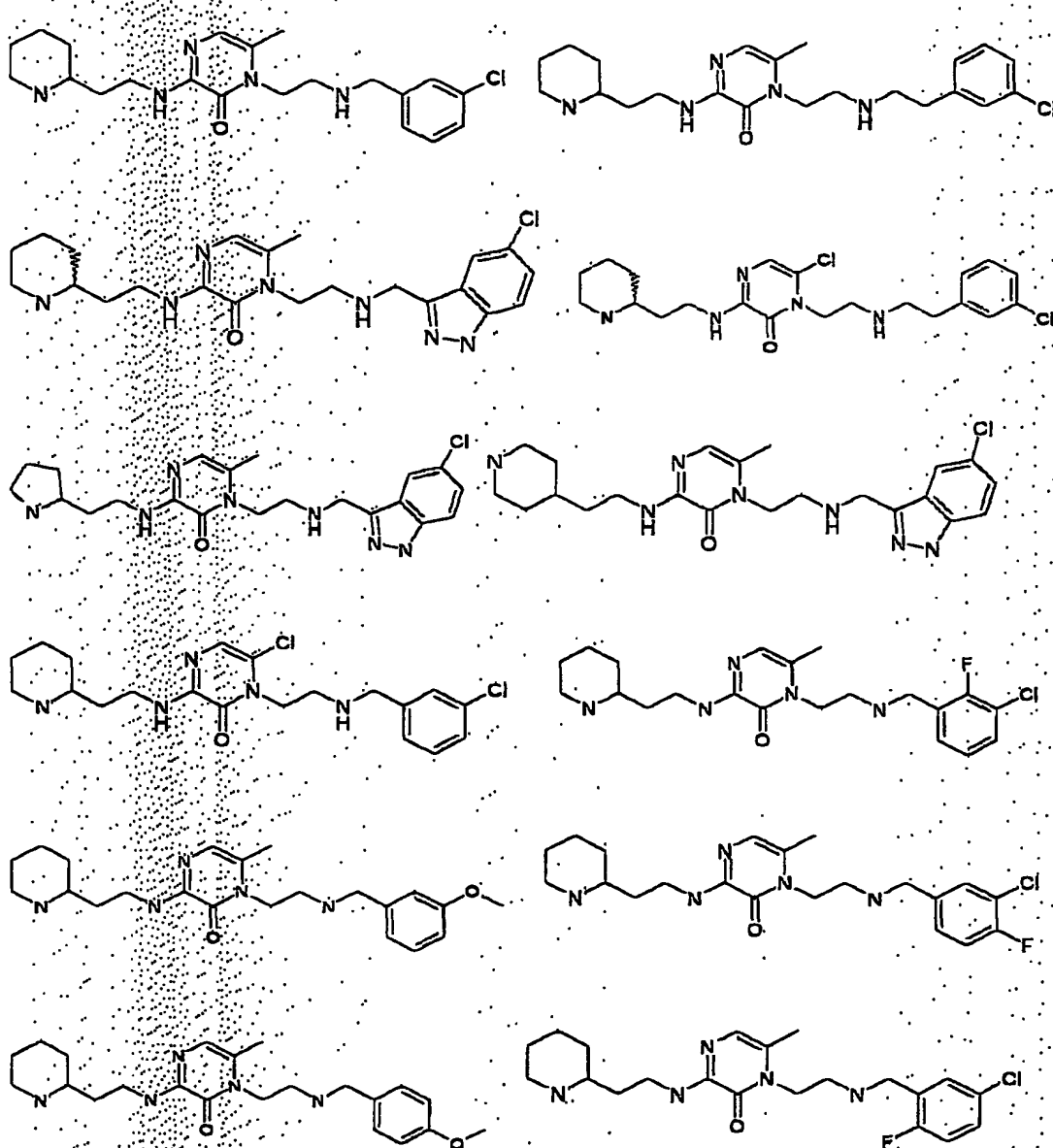


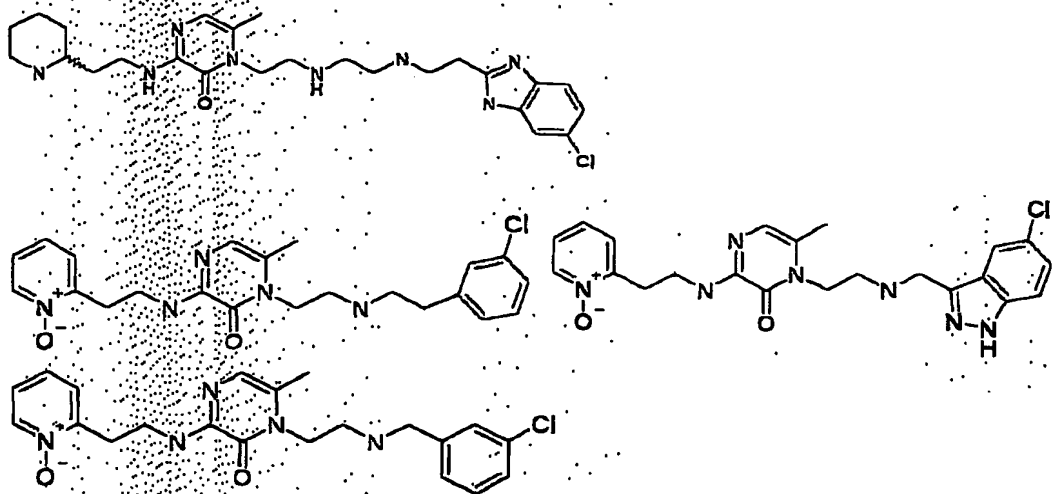












24. A prodrug of a compound according to any one of the claims 1 to 23.
25. A pharmaceutical composition comprising a compound or a mixture of compounds or a pharmaceutically acceptable salt thereof according to any one of the claims 1 to 23 together with a pharmaceutically acceptable carrier.
26. A pharmaceutical composition comprising a prodrug according to claim 24 or a mixture of prodrugs or prodrugs and compounds according to any one of the claims 1 to 23 or a pharmaceutically acceptable salt together with a pharmaceutically acceptable carrier.
27. A pharmaceutical composition according to claim 25 or 26, additionally comprising one or more known anticoagulants.
28. A compound or a pharmaceutically acceptable salt of any one of the claims 1 to 23 for use as a medicament.
29. A prodrug or a pharmaceutically acceptable salt of claim 24 for use as a medicament.
30. Use of a compound or a pharmaceutically acceptable salt of any of the claims 1 to 23 for the manufacture of a medicament for the treatment or prophylaxis of thromboembolism, thrombosis, arteriosclerosis, unstable angina, refractory angina, myocardial infarction, transient ischemic attacks, atrial fibrillation, thrombotic stroke, embolic stroke, deep vein

thrombosis, disseminated intravascular coagulation, ocular build up of fibrin, and reocclusion or restenosis of recanalized vessels.

31. Use of a prodrug or a pharmaceutically acceptable salt of claim 24 for the manufacture of a medicament for the treatment or prophylaxis of thromboembolism, thrombosis, atherosclerosis, unstable angina, refractory angina, myocardial infarction, transient ischemic attacks, atrial fibrillation, thrombotic stroke, embolic stroke, deep vein thrombosis, disseminated intravascular coagulation, ocular build up of fibrin, and reocclusion or restenosis of recanalized vessels.

32. Use of a compound according to any one of the claims 1 to 23 or a prodrug according to claim 24 as an anticoagulant or thrombin inhibitor.

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

☐ BLACK BORDERS

☒ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES

☒ FADED TEXT OR DRAWING

☒ BLURRED OR ILLEGIBLE TEXT OR DRAWING

☐ SKEWED/SLANTED IMAGES

☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS

☐ GRAY SCALE DOCUMENTS

☒ LINES OR MARKS ON ORIGINAL DOCUMENT

☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY

☐ OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.